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IN THE UNITED STATES PATENT AND TRADEMARK OFFICE

Applicant:	Vassilis I. Zannis et al.	Art Unit:	1636
Serial No.:	09/827,854	Examiner:	Nguyen, Q.
Filed:	April 5, 2001	Customer No.:	21559
Title:	COMPOUNDS AND METHODS FOR LOWERING CHOLESTEROL LEVELS WITHOUT INDUCING HYPERTRIGLYCERIDEMIA		

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DECLARATION OF DR. VASSILIS I. ZANNIS, Ph.D.
UNDER 37 C.F.R. § 1.132

I, VASSILIS I. ZANNIS, declare:

1. I am a named inventor of the subject matter claimed in United States Patent Application Serial No. 09/827,854 filed on April 5, 2001.

2. I attended the University of California at Berkley where I obtained a Ph.D. in Biochemistry. I am currently a Professor in the department of Medicine and Biochemistry and the Director of Molecular Genetics at the Whitaker Cardiovascular Institute associated with the Boston University School of Medicine. My education and professional experience include PhD in biochemistry from the University of California at Berkeley in 1975, followed by postdoctoral training during the 1975-1982 period at the University of California at San Francisco, MIT and Harvard Medical School.

In 1982 I became Assistant Professor in Pediatrics/Biochemistry at Harvard Medical School. In 1984 I was recruited as Associate Professor to Boston University School of Medicine to start a new section of Molecular Genetics, and I was promoted to full Professor in 1987. My current position is Professor of Medicine and Biochemistry and Director of Molecular Genetics at Boston University School of Medicine.

Since 1978, my research has focused in the field of lipoprotein research and genetic abnormalities that are associated with lipid disorders. Since 1978 I have published 115 original articles and 37 reviews on the subject of lipoproteins (out of a total of 125 publications and 40 reviews in my CV), and there are over 5,000 citations of my work.

Major past contributions include the elucidation of the apoE polymorphism that generates the common isoforms in humans (apoE2, apoE3 and apoE4; apoE2 is associated with cardiovascular disease, and apoE4 is associated with Alzheimer's disease), the clonic characterization and expression of most the apolipoproteins, cDNAs and genes (including that of apoB), as well as in-depth analysis of the regulation of these genes.

My current research focuses on the following areas:

- Apolipoprotein gene regulation *in vivo* using antisense and transgenic methodologies and adenovirus-mediated gene transfer and comparative genomics.
- Elucidation of the structure-function relationship of human apoA-I and apoE and their relevance to cardiovascular disease and Alzheimer's disease respectively, using *in vitro* mutagenesis, transgenic and gene transfer methodologies. Pertinent questions are the role of apoA-I in the biogenesis and the functions of HDL, the role of apoE in atheroprotection and in cholesterol and triglyceride homeostasis in the circulation, the role of apoE in lipid homeostasis in the brain, and the pathogenesis of Alzheimer's disease.

3. I have read and understood the Office Action, dated January 25, 2005. This Declaration is presented to overcome the rejection of claims 30-31, 33-34, 36-37, 43-44, 46-47, 50-51, 53-62, 64-72, 74, and 76-78 under 35 U.S.C. § 112, first paragraph, for lack of enablement.

4. The methods of the invention have been used successfully and predictably to demonstrate expression of an apoE polypeptide lacking amino acids 260-299 in an apoE-/- mouse model following intravascular administration using an adenoviral vector. Expression of the apoE polypeptide lacking amino acids 260-299 in the mice resulted in a reduction in serum cholesterol levels without a concomitant increase in triglycerides.

5. The experiments described in the specification were successfully performed in a mouse model using an adenoviral vector, which is accepted by skilled artisans working in the field of gene therapy as predictive of success in humans. The skilled artisan would also conclude, based on pre- and post-filing art, that the successful reduction in serum cholesterol levels without a concomitant increase in triglycerides achieved in the mouse model would again be predictive of success for the treatment of hypercholesterolemia in humans.

6. Based on the results of the experiments disclosed in the specification, I concluded that this method would be useful for the treatment of hypercholesterolemia in humans without causing hypertriglyceridemia. Furthermore, I believe that it is reasonable to conclude that one skilled in the art would also reasonably draw this conclusion.

7. I hereby declare that all statements made herein of my own knowledge are true and that all statements made on information and belief are believed to be true; and further that these statements were made with the knowledge that willful false statements and the like so made are punishable by fine or imprisonment, or both, under Section 1001 of Title 18 of the United States Code and that such willful false statements may jeopardize the validity of the application or any patents issued thereon.

Respectfully submitted,

Date: 7/22/2005

Vassilis I Zannis

Vassilis I. Zannis, Ph.D.